Micronuclei As Biomarkers Of Genetic Damage In Oral Squamous Cell Carcinoma†

Nancy A. Shaaban1* BDS, Hanaa S. Raslan1 PhD, Omneya M. Ramadan1 PhD, Ahmed S. Habib2 PhD, Eiman I. Zaki3 PhD

1. Oral Pathology Department, Faculty of Dentistry, Alexandria University, Egypt 2. Cranio Maxillofacial and Plastic Surgery Department, Faculty of Dentistry, Alexandria University, Egypt 3. Histology and Cell Biology Department, Faculty of Medicine, Alexandria University, Egypt

*Corresponding author

Introduction

• Oral cancer is a major health problem, causing high morbidity and mortality rates. Oral Squamous Cell Carcinoma (OSCC) accounts for 90-95% of all oral malignancies. The prognosis of OSCC is often poor due to the late discovery of most lesions, after they have reached a large size. Hence the importance of early diagnosis of cancer which raises the five year survival rate to 90% as opposed to 20% in case of late diagnosis. Here comes the role of biomarkers of genetic damage that can have a patient utility in early diagnosis of cancer. Many investigators have already called micronuclei (MN) an upcoming biomarker of tumorigenesis as it is considered an objective, non-invasive method for early detection of genetic damage. More than 90% of human malignancies originate from epithelial cells. Thus the MN test in exfoliated buccal epithelial cells could be used as a tool for biomonitoring the genetic damage in high risk human populations and for screening cellular alteration in OSCC cases.

Objectives

• The study aimed to assess the degree of genetic damage in the oral squamous cell carcinoma lesions and their adjacent mucosa using micronuclei as biomarkers in cytological smears.
• To correlate cytological smear results with histopathological findings of oral squamous cell carcinoma lesions.

Methods

I. Sample
• A total of 34 participants; 17 OSCC patients and 17 healthy control subjects were included.

II. Cytological study
• Cytological smears were taken from the OSCC cases as well as from the buccal mucosa of the control subjects using a cytobrush. Cytological smears were stained using Papanicolaou stain. The micronucleated (MNed) cells were identified according to the criteria established by Tolbert et al. and were counted per 1000 cells.

III. Histological examination
• Biopsies were taken from the tumor tissue and stained using Hematoxylin and Eosin (H&E) to confirm the diagnosis. The histologic grade was determined.

1st: Cell inclusion criteria

- Little or no overlap with preexistent cells
- Cell, thin as a wallof the nucleus

2nd: Micronucleated Cell Characterization

- Micronucleated cell without a membrane or dividing a membrane
- Micronucleated cell characterisation

Results

1. Clinical results:
• The mean age for the recorded SCC cases was (57.24 years) with a range from 43-75 years. The mean age for the healthy control cases was (30.71 years) with a wide range from 17-61 years. The most common site of occurrence was the alveolar ridge, 6 cases (35.3%), followed by the lateral border of the tongue, 5 cases (29.4%) and the buccal mucosa 4 cases (23.5%). On the other hand the least frequent site of occurrence was the lip, just two cases (11.8%).

2. Histopathological Results:
• The microscopic examination for the cases of squamous cell carcinoma revealed that 3 cases (17.6%) were of well differentiated type, 12 cases (70.6%) were moderately differentiated, and 2 cases (11.8%) were of the poorly differentiated type.

3. Cytological smears Results
• The mean frequency of MNi in healthy control subjects was 18.69 MNed cells/1000 cells.
• Well differentiated SCC (n=3) Mean frequency was 57.71 MNed cells/1000 cells in the lesion while in the adjacent healthily appearing mucosa it was found to be 63.82 MNed cells/1000 cells.
• Moderately differentiated SCC (n=11) Mean frequency was 29.69 MNed cells/1000 cells in the lesion while in the adjacent healthily appearing mucosa it was found to be 36.44 MNed cells/1000 cells.
• In the poorly differentiated SCC cases (n=2) Mean frequency was 86.52 MNed cells/1000 cells in the lesion while in the adjacent healthily appearing mucosa it was found to be 84.82 MNed cells/1000 cells.

4. Correlating Mean Micronuclei Frequency in Squamous Cell Carcinoma, Adjacent Healthy Mucosa and Healthy Controls:
• The highest frequency was in the healthy mucosa of SCC cases (47.62±26.51) while the lowest was in control cases with mean frequency (18.69±11.16).

5. Correlating Micronuclei Frequency in Cytological Smears and the Corresponding Histopathological Grade
• The greatest MNi frequency was recorded in the lesion area of poorly differentiated SCC (86.52±60.0), Whereas the lowest value was recorded in the lesion area of moderately differentiated squamous cell carcinoma (29.69±12.12).

Conclusions

• This study concluded that MNi can reliably be used as a as a biomarker of genetic damage as their mean frequency was significantly higher in OSCC patients than healthy controls. The significant increase in MNi frequency from moderately differentiated OSCC to poorly differentiated OSCC indicates its progressive increase with the increase in the degree of genetic damage.
• Moreover, the mean MNi frequency was significantly higher in the area of clinically healthy mucosa adjacent to the main tumor in OSCC patients than in healthy controls thus yielding strength to the hypothesis of field cancerization. Field cancerization may be the reason behind regional recurrences and secondary primary tumors thus its early detection may aid in decreasing morbidity and mortality rates.

References


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